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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/009,254 | 06/17/2002 | Elisabeth E. Adderson | 1321.2.29.1 | 8298 |

21552 7590 11/21/2005

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| EXAMINER | |
|---|---|
| DEVI, SARVAMANGALA J N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/009,254 | ADDERSON ET AL. | |
| | Examiner | Art Unit | |
| | S. Devi, Ph.D. | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *17-32, 38-55 and 61-67* is/are withdrawn from consideration.

5)☒ Claim(s) *1-16 and 56* is/are allowed.

6)☒ Claim(s) *33-37 and 57-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

# RESPONSE TO APPLICANTS' AMENDMENT

## Applicants' Amendment

**1)** Acknowledgment is made of Applicants' amendment filed 09/16/05 in response to the non-final Office Action mailed 03/17/05.

## Status of Claims

**2)** Claims 1, 6-8, 14-16, 33 and 57 have been amended via the amendment filed 09/16/05.

Claims 1-67 are pending.

Claims 1-16, 33-37 and 56-60 are under examination.

## Prior Citation of Title 35 Sections

**3)** The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

## Prior Citation of References

**4)** The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

## Rejection(s) Withdrawn

**5)** The rejection of claims 6, 14 and those dependent therefrom made in paragraph 7 of the Office Action mailed 03/17/05 under 35 U.S.C § 101 as being directed to a non-statutory subject matter, is withdrawn in light of Applicants' amendment to the claims.

**6)** The rejection of claims 6-8 and 14-16 made in paragraph 9 of the Office Action mailed 03/17/05 under 35 U.S.C. § 112, first paragraph, as being non-enabled with regard to the scope, is in light of Applicants' amendment to the claims.

**7)** The rejection of claim 1 made in paragraph 11(a) of the Office Action mailed 03/17/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

**8)** The rejection of claims 33 and 57 made in paragraph 11(b) of the Office Action mailed 03/17/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

**9)** The rejection of claims 2-16, 34-37 and 58-60 made in paragraph 11(c) of the Office Action mailed 03/17/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim(s).

## Rejection(s) Maintained

**10)** The rejection of claims 33-37 and 57-60 made in paragraph 8 of the Office Action mailed 03/17/05 under 35 U.S.C. § 112, first paragraph, as being non-enabled, is maintained for reasons set forth therein and herebelow.

Applicants argue that while it might require several minimally-trained technicians some time to identify the most antigenic fragment of spb1 and further determine the optimal dosage to elicit an immune response, such a process could be done with relative straightforward ease. Applicants submit that vaccines are routinely made all the time with very little effort expended on optimizing the antigenicity. Applicants state that typically whole organisms are even used with no thought of optimization. Applicants submit that routine experimentation may be required to practice the subject matter of the claims, but urge that the issue of undue experimentation is not to be confused with routine experimentation.

Applicants' arguments have been carefully considered, but are not persuasive. Applicants are correct in that only routine experimentation is needed by those of skill in the art to establish the antigenicity of the recited protein. However, it is important to note that what is being claimed is not an 'antigenic composition' comprising an isolated and purified protein, or a non-isolated and non-purified protein comprising the amino acid sequence of SEQ ID NO: 2, and a method of 'raising antibodies' in a mammal to the said protein. On the contrary, the instant claims are drawn to a 'vaccine for immunizing a mammalian host against virulent Group B streptococcal infection' comprising an isolated and purified protein comprising the amino acid sequence of SEQ ID NO: 2, and a method of 'immunizing a mammal against Group B streptococcal infection, said method comprising administering to the mammal a vaccine comprising an immunologically effective amount of a recombinantly produced protein comprising the amino acid sequence of SEQ ID NO: 2'. As set forth previously at paragraph 8 of the Office Action mailed 03/17/05, the term 'vaccine' by definition requires that the claimed element in the vaccine elicit a protective immune response, humoral and/or cell mediated, in a suitable host who is susceptible against pathogens that produce or carry such element. A vaccine 'must by definition trigger an immunoprotective response in the

host vaccinated; mere antigenic response is not enough'. *In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).* In the instant case, the active element in the vaccine is the protein of the amino acid sequence, SEQ ID NO: 2, which is required to be 'immunoprotective' against a Group B streptococcal infection. The phrase 'Group B streptococci infection' broadly encompasses GBS types I, II, III, V, VIII etc. A review of the instant specification indicates the following. At page 7, the specification states that: (a) The *spbl* gene product 'may stimulate an immune response' when administered to a host; (b) Recombinantly produced proteins are especially desirable, as they can be produced in large amounts and purified; (c) Recombinantly produced proteins 'may' be engineered to maximize desirable activities and to minimize unwanted effects; and (d) The recombinantly produced *spbl* and/or *spb2* gene products 'may be' used as carrier proteins for a polysaccharide-protein or oligosaccharide-protein conjugate vaccine. At page 12, the specification states that *spbl* is not a member of a significantly homologous "family" of genes. It is further stated that the 53 kD protein is a predicted protein product having the characteristics of a typical gram positive cell-wall bound protein. Based on segmental homology alone with *Actinomyces* fimbrial proteins and *H. influenzae* HMW1, the specification speculates that 'Spb1 might contribute to GBS adhesion or invasion'. Applicants state that a *spb1*$^-$ isogenic deletion mutant GBS strain was created by homologous recombination and that the number of *spb1*$^-$ bacteria adherent to A549 monolayers was reduced by 60.0% and the number of intracellular invading bacteria was reduced by 53.6%. With this, Applicants concluded that 'Spb1 may contribute to the pathogenesis of GBS pneumonia and bacterial entry into the blood stream'. However, there is no showing within the instant specification that the protein comprising the amino acid sequence of SEQ ID NO: 2 was indeed produced, isolated and purified, that too recombinantly produced, such that an immunologically effective amount of the same served as a 'vaccine' in a mammal and conferred immunoprotection against the generically recited virulent Group B streptococcal infection. The 53 kD protein is described as the predicted spb1 protein product (see page 12). There is absolutely no showing that a 'recombinantly produced protein comprising the amino acid sequence of SEQ ID NO: 2' or an 'isolated and purified protein comprising the amino acid sequence of SEQ ID NO: 2' was administered to any mammal as a vaccine wherein the vaccine provided 'immunoprotection' against, or reduced the mortality or morbidity of the disease caused by, pathogenic GBS in said mammal. This is critically important because it is well known in the art

that, of a myriad of polypeptides that may be produced by a bacterial or microbial pathogen, not all polypeptides elicit a pathogen-specific immune response that is protective against the pathogen. The art of vaccines recognizes the unpredictability associated with whether or not an antigen or immunogenic component derived from a microbial pathogen is immunoprotective. For instance, Ellis RW (*Vaccines*, (Eds) Plotkin *et al.*, W.B. Saunders Company, Philadelphia, Chapter 29, 568-575, 1988, see page 571, second full paragraph – already of record) reflected this problem in the teaching that the key to the problem of vaccine development "is the identification of that protein component of a ..... microbial pathogen that itself can elicit the production of protective antibodies ..... and thus protect the host against attack by the pathogen". It is emphasized that predictability or unpredictability is one of the *Wands* factors for enablement. In the instant case, the claimed protein, in isolated, purified or recombinant form, is not evaluated for its protective capacity against any GBS infection using an art-accepted *in vivo* animal model, nor are there any *in vitro* test results correlative of protection against any GBS infection. Furthermore, the protective nature of a recombinantly produced bacterial protein is not predictable. The art recognizes the unpredictability associated with the protective ability of a recombinantly produced bacterial protein. For instance, Manetti *et al.* (*Infect. Immun.* 63: 4476-4480, November 1995, already of record) explicitly demonstrated that a recombinant *Helicobacter pylori* CT protein "lacked any biological activity" and failed to induce antibodies that are neutralizing. Such a recombinant protein would be unlikely to have the ability to induce useful antibodies to virulent GBS and is unlikely to serve as a prophylactic or therapeutic vaccine. Absent a concrete showing that the claimed product is effective in protecting against any GBS infection in any mammal, or eliminating or reducing morbidity and/or mortality due to GBS infections, the claims drawn to a vaccine and method immunizing a mammal against Group B streptococcal infection by administering the vaccine against GBS infection are considered non-enabled. Therefore, undue experimentation would have been required by one of skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of specific and adequate disclosure, the lack of working examples, the art-demonstrated unpredictability, the quantity of experimentation necessary, and the breadth of claims. *Ex parte Foreman*, 230 USPO 546, 547 (Bd. Pat. Appls. and Inter. 1986). The claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph. The rejection stands.

## Remarks

**11)** Claims 33-37 and 57-60 stand rejected. Claims 1-16 and 56 are allowed.

**12)** **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**13)** Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (571) 273-8300.

**14)** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**15)** Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

November, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER